

## WHAT IS CLAIMED IS

1. A method for detecting a pain-regulating substance comprising the steps of:
  - (a) incubating a test substance with a biomolecule selected from group I, wherein group I consists of the protein BNPI or DNPI or a protein comprising SEQ ID NO: 2, 4, 6, 8, 10, 12 or 14 or a protein which is at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or a polynucleotide which is at least 90% homologous thereto, or a protein encoded by a nucleic acid which binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or antisense polynucleotides thereof, or a part protein of one of the abovementioned proteins which is at least 10 amino acids long or a cell or a preparation from a cell which has synthesized at least one of the abovementioned proteins or part proteins and
  - (b) measuring the binding of the test substance to the protein or part protein synthesized by the cell or measuring at least one functional parameter modified by the binding of the test substance to the protein or part protein.
2. A method according to claim 1, wherein the cell is manipulated by genetic engineering before step (a).

3. A method according to claim 2, wherein the manipulation by genetic engineering allows the measurement of at least one functional parameter modified by the binding of the test substance.
4. A method according to claim 3, wherein the manipulation by genetic engineering causes expression of a form of a G protein which is not expressed endogenously in the cell or introduction of a reporter gene.
5. A method according to claim 2, wherein the cell is manipulated by genetic engineering so that the cell contains at least one polynucleotide selected from the group consisting of SEQ ID NOS: 1, 3, 5, 7, 9, 11 and 13, or a polynucleotide which is at least 90% homologous thereto.
6. A method according to claim 5, wherein the polynucleotide is contained in a recombinant DNA construct.
7. A method according to claim 2, wherein after the manipulation by genetic engineering according to claim 2 and before step (a), the cell is cultured under conditions which allow expression.
8. A method according to claim 7, wherein the cell is cultured under selection pressure.
9. A method according to claim 1, wherein the cell is an amphibia cell, bacteria cell, yeast cell, insect cell or an immortalized or native mammalian cell.

10. A method according to claim 1, wherein the measurement of the binding is carried out via the displacement of a known labeled ligand of the part protein or protein or via the activity bound thereto from a labeled test substance.
11. A method according claim 1, wherein the measurement of at least one functional parameter modified by the test substance is carried out via measurement of the regulation, inhibition or activation of receptors, ion channels or enzymes.
12. A method according claim 1, wherein the measurement of at least one functional parameter modified by the test substance is carried out via measurement of the modification of the gene expression, the ionic medium, the pH, the membrane potential, the enzyme activity or the concentration of the second messenger.
13. A method according to claim 1, in which a first method according to claim 1 is coupled with a second method according to claim 1 such that the measurement values and results of the first method in respect of the substance to be measured are compared with the measurement values and results of the second method in respect of the substance to be measured, wherein one of the two methods is the main method, wherein, in step (a) of said main method, the substance to be tested is incubated either  
with a biomolecule selected from group II, wherein group II consists of the the protein BNPI or a protein comprising SEQ ID NO: 2, 4, 6 or 8 or a protein which is at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 1, 3, 5 or 7 or a polynucleotide

which is at least 90% homologous thereto, or a protein encoded by a nucleic acid which binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 1, 3, 5 or 7 or antisense polynucleotides thereof, or a part protein of one of the abovementioned proteins which is at least 10 amino acids long or a cell or a preparation from a cell which has synthesized at least one of the abovementioned proteins or part proteins, or

with a biomolecule selected from group III, wherein group III consists of the protein DNPI or a protein comprising SEQ ID NO: 10, 12 or 14, or a protein which at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 9, 11 or 13 or a polynucleotide which is at least 90% homologous thereto, or a protein encoded by a nucleic acid which binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 9, 11 or 13 or antisense polynucleotides thereof, or a part protein of one of the abovementioned proteins which is at least 10 amino acids long or a cell or a preparation from a cell which has synthesized at least one of the abovementioned proteins or part proteins, and

wherein, in a secondary method, in step (a) the substance to be tested is incubated with a biomolecule from group I or with a biomolecule selected from group II or group III, wherein the biomolecule selected from group II or group III is selected from a group which differs from group the biomolecule with which the substance in the main method is incubated.

14. A method according to claim 1, wherein the pain regulated by the substance to be detected is selected from the group consisting of: chronic pain, neuropathic pain, mechanical hyperalgesia, diabetic neuropathy; visceral pain, cerebral pain, peripheral pain, inflammation-

related pain, migraine, cluster headache or pain with trigeminal neuralgia.

15. The method of claim 14, wherein said pain is either musculoskeletal pain, allodynic pain or peripheral inflammation pain.
16. A compound identifiable as a pain-regulating substance by a method according to claim 1.
17. A compound according to claim 16, wherein said compound is a low molecular weight compound.
18. A method of alleviating pain comprising administering an effective pain alleviating amount of:
  - a. a polynucleotide which codes for BNPI or DNPI or a polynucleotide which is at least 90% homologous to one of the nucleotide sequences comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13,
  - b. a polynucleotide with a nucleotide sequence which is capable of binding specifically to one of the polynucleotides listed under point a),
  - c. a vector containing a polynucleotide according to one of points a) or b),
  - d. BNPI or DNPI or a protein comprising SEQ ID NO: 2, 4, 6, 8, 10, 12 or 14 or a protein which is at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13) or a polynucleotide which is at least 90% homologous thereto, or a protein encoded by a nucleic acid which

binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or antisense polynucleotides thereof or a part protein of one of the abovementioned proteins which is at least 10 amino acids long,

- e. an antibody, against one of the proteins or part proteins according to point d),
- f. a cell, containing a polynucleotide according to one of points a) or b), a vector according to point c), a protein or part protein according to point d) or an antibody according to point e)
- g. a compound according to claim 16 or
- h. an active compound, preferably a low molecular weight active compound, which binds to a protein or part protein according to point a), and

at least one carrier or auxiliary substance.

- 19. A method according to claim 18, wherein the pain is selected from the group consisting of:  
chronic pain, neuropathic pain, mechanical hyperalgesia, diabetic neuropathy; visceral pain, cerebral pain, peripheral pain, inflammation-related pain, migraine, cluster headache or pain with trigeminal neuralgia.
- 20. The method of claim 19, wherein said pain is either musculoskeletal pain, allodynic pain or peripheral inflammation pain.
- 21. A method of providing gene therapy to a mammal, said method comprising administering to said mammal a therapeutic amount of:

- a. a polynucleotide which codes for BNPI or DNPI or a polynucleotide which is at least 90% homologous to a nucleotide sequence comprising SEQ ID NO: 1, 3, 5 or 7,
  - b. a polynucleotide which is capable of binding specifically to one of the polynucleotides listed under point a),
  - c. a vector comprising a polynucleotide according to one of points a) or b), or
  - f. a cell containing a polynucleotide according to one of points a) or b) or a vector according to point c).
22. The method of claim 21, wherein said gene therapy is *in vivo* gene therapy.
23. The method of claim 21, wherein said gene therapy *in vitro* gene therapy.
24. The method of claim 21, wherein said gene therapy is effective in alleviating pain.
25. A method according to claim 21, wherein the pain is selected from the group consisting of:  
chronic pain, neuropathic pain, mechanical hyperalgesia, diabetic neuropathy; visceral pain, cerebral pain, peripheral pain, inflammation-related pain, migraine, cluster headache or pain with trigeminal neuralgia.
26. The method of claim 25, wherein said pain is either musculoskeletal pain, allodynic pain or peripheral inflammation pain.

27. A method of diagnosing a pain state comprising administering an effective amount of a diagnostic agent comprising:
- a. a polynucleotide which codes for BNPI or DNPI or a polynucleotide which is at least 90% homologous to a nucleotide sequence comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13,
  - b. a polynucleotide capable of binding specifically to one of the polynucleotides listed under point a),
  - c. a vector comprising a polynucleotide according to one of points a) or b),
  - d. BNPI or DNPI or a protein comprising SEQ ID NO: 2, 4, 6, 8, 10, 12 or 14 or a protein which at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or a polynucleotide which is at least 90% homologous thereto, or a protein encoded by a nucleic acid which binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or antisense polynucleotides thereof or a part protein of one of the abovementioned proteins which is at least 10 amino acids long,
  - e. an antibody against one of the proteins or part proteins according to point d),
  - f. a cell containing a polynucleotide according to one of points a) or b), a vector according to point c), a protein or part protein according to point d) or an antibody according to point e)
  - g. a compound according to claim 16 or
  - h. an active compound, preferably a low molecular weight active compound, which binds to a protein or part protein according to point a), and



detecting an indicator affected by the diagnostic agent.

28. A method according to claim 27, wherein the pain state is selected from the group consisting of:  
chronic pain, neuropathic pain, mechanical hyperalgesia, diabetic neuropathy; visceral pain, cerebral pain, peripheral pain, inflammation-related pain, migraine, cluster headache or pain with trigeminal neuralgia.
29. The method of claim 28, wherein said pain state is either musculoskeletal pain, allodynic pain or peripheral inflammation pain.
30. A method of detecting a pain-regulating substance comprising administering an effective amount of a diagnostic agent comprising:
  - a. a polynucleotide, which codes for BNPI or DNPI or a polynucleotide, which is at least 90% homologous with a nucleotide sequence comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13,
  - b. a polynucleotide which is capable of binding specifically to one of the polynucleotides listed under point a),
  - c. a vector containing a polynucleotide according to one of points a) or b),
  - d. BNPI or DNPI or a protein comprising SEQ ID NO: 2, 4, 6, 8, 10, 12 or 14 or a protein which at least 90% homologous thereto or a protein encoded by a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or a polynucleotide which at least 90% homologous thereto, or a protein which encoded by a nucleic acid which binds under stringent conditions to a polynucleotide comprising SEQ ID NO: 1, 3, 5, 7, 9, 11 or 13 or

- antisense polynucleotides thereof or a part protein of one of the abovementioned proteins which is at least 10 amino acids long,
- e. an antibody against one of the proteins or part proteins according to point d),
  - f. a cell containing a polynucleotide according to one of points a) or b), a vector according to point c), a protein or part protein according to point d) or an antibody according to point e), and
- detecting an indicator affected by the diagnostic agent.

- 31. A method according to claim 30, wherein the pain regulated by said pain-regulating substance is selected from the group consisting of: chronic pain, neuropathic pain, mechanical hyperalgesia, diabetic neuropathy; visceral pain, cerebral pain, peripheral pain, inflammation-related pain, migraine, cluster headache or pain with trigeminal neuralgia.
- 32. The method of claim 31, wherein said pain is either musculoskeletal pain, allodynic pain or peripheral inflammation pain.